

MEA-System Manual



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Table of Contents

1	Important Information and Instructions	5
1.1	Operator's Obligations	5
1.2	Guarantee and Liability	5
1.3	Important Safety Advice	6
2	Welcome to MEA-Systems	9
2.1	Basic Components of MEA-Systems	9
2.2	System Configurations and Optional Components	10
2.2.1	Single Components for Standard-Systems	10
2.2.2	Enhanced Perfusion-System (-E)	10
2.2.3	MEA1060-BC Amplifier with Stimulus Artifact Suppression	11
2.2.4	MEA60 and MEA120-System	11
2.2.5	MEA Switch for Using Additional Amplifiers	11
2.3	Accessories	11
2.4	Add-ons for Stimulation	12
2.5	Setting Up the MEA-System	12
2.6	Supply Power and Recommended Setups	13
3	Extracellular Recording From MEAs	14
3.1	Introduction	14
3.2	Background	14
3.3	Signal types	15
3.3.1	Single Unit Activities	15
3.3.2	Local Field Potentials	15
3.4	Recording and Stimulation	15
3.4.1	Microelectrode Arrays (MEAs)	16
3.4.2	Signal Amplification and Filters	16
3.4.3	Data Acquisition	17
3.5	Using the Additional Analog Inputs	20
3.5.1	Recording Voice on Analog Inputs	20
3.6	Digital Input/Output, System Synchronization	20
3.6.1	Triggering the MC_Card and MC_Rack	20
3.6.2	Custom Switch for "Remote-Controlling" of the MC_Card	21
3.6.3	Triggering Other Instruments by the MC_Card	21
4	Troubleshooting	22
4.1	About Troubleshooting	22
4.2	Triggering / Digital Input Does not Work	22
4.3	Artifacts Caused by Perfusion	23

5	Appendix	25
5.1	Contact Information	25
5.2	Ordering Information	26
5.2.1	MEA-Systems	26
5.2.2	MEA Amplifiers	27
5.2.3	Accessories	27
5.2.4	Stimulus Generators	28

1 Important Information and Instructions

1.1 Operator's Obligations

The operator is obliged to allow only persons to work on the device, who

- are familiar with the safety at work and accident prevention regulations and have been instructed how to use the device;
- are professionally qualified or have specialist knowledge and training and have received instruction in the use of the device;
- have read and understood the chapter on safety and the warning instructions in this manual and confirmed this with their signature.

It must be monitored at regular intervals that the operating personnel are working safely.

Personnel still undergoing training may only work on the device under the supervision of an experienced person.

1.2 Guarantee and Liability

The *General conditions of sale and delivery* of **Multi Channel Systems** MCS GmbH always apply. The operator will receive these no later than on conclusion of the contract.

Multi Channel Systems MCS GmbH makes no Guarantee as to the accuracy of any and all tests and data generated by the use of the device or the software. It is up to the user to use good laboratory practice to establish the validity of his findings.

Guarantee and liability claims in the event of injury or material damage are excluded when they are the result of one of the following.

- Improper use of the device
- Improper installation, commissioning, operation or maintenance of the device
- Operating the device when the safety and protective devices are defective and/or inoperable
- Non-observance of the instructions in the manual with regard to transport, storage, installation, commissioning, operation or maintenance of the device
- Unauthorized structural alterations to the device
- Unauthorized modifications to the-System settings
- Inadequate monitoring of device components subject to wear
- Improperly executed and unauthorized repairs
- Unauthorized opening of the device or its components
- Catastrophic events due to the effect of foreign bodies or acts of God

1.3 Important Safety Advice



Warning: ME- / MEA-Systems include several instruments as individual components. Each instrument is shipped with a separate Manual. The information in the individual Manuals fully apply to the complete-System. This manual is only to be understood as an additional information. Read all Manuals thoroughly before setting up the system.



Warning: Obey always the rules of local regulations and laws. Only qualified personnel should be allowed to perform laboratory work. Work according to good laboratory practice to obtain best results and to minimize risks.

The product has been built to the state of the art and in accordance with recognized safety engineering rules. The device may only

- be used for its **intended purpose**;
- be used when in a **perfect condition**.
- Improper use could lead to serious, even fatal injuries to the user or third parties and damage to the device itself or other material damage.



Warning: The devices and the software are **not** intended for medical uses and **must not be used on humans**.

Malfunctions which could impair safety should be rectified immediately.

High Voltage

Electrical cords must be properly laid and installed. The length and quality of the cords must be in accordance with local provisions.

Only qualified technicians may work on the electrical system. It is essential that the accident prevention regulations and those of the employers' liability associations are observed.

- Each time before starting up, make sure that the **mains supply** agrees with the specifications of the products.
- Check the **power cords** for damage each time the site is changed. Damaged power cords should be replaced immediately and may never be reused.
- Check the **leads** for damage. Damaged leads should be replaced immediately and may never be reused.
- Do not try to insert anything sharp or metallic into the vents or the case of the products.
- Liquids may cause short circuits or other damage. Keep the devices and the power cords always **dry**. Do **not** handle it with wet hands.

Electromagnetic compatibility of the MC_Card

The MC_Card data acquisition board is only intended for research work in laboratories. It belongs to product class 0 conforming to the European Product Regulations and the CE (Conformité Européenne) marking. The MC_Card complies with all applicable directives specified in the Council Directive for Electromagnetic Compatibility (89/336/EU).

Requirements for the installation

- The MC_Card is only suitable for extra-low voltages and shall be used only as specified.
- The equipment shall be correctly earthed or connected to the ground.
- The analog inputs should be closed or connected to active signals.
- Connections to all inputs and outputs shall be made with screened cables specified by Multi Channel Systems. The screen has to be connected to a solid earth or chassis connection. ESD voltages at open lines may cause malfunction during operation.
- The products shall only be operated from approved power packs (if necessary).

2 Welcome to MEA-Systems

2.1 Basic Components of MEA-Systems



Multi Channel Systems provides complete solutions for **stimulation, perfusion, recording, and data acquisition** from up to **128** channels, data analysis and export. The **MEA (microelectrode array)** product line is intended for extracellular electrophysiological recordings *in vitro*. Applications include whole-heart preparations; acute brain, heart, and retina slices; cultured slices; and dissociated neuronal or cardiomyocyte cell cultures.

In the following, all basic components that are part of all complete MEA-Systems are briefly described.

A microelectrode array is an arrangement of **60 electrodes** that allows the simultaneous targeting of several sites for extracellular stimulation and recording. Cell lines or tissue slices are placed directly on the MEA and can be cultivated for up to several months. Almost all excitable or spontaneously active cells and tissues can be used. The **temperature controller TC01/02** regulates the MEA temperature.

Raw data from the MEA electrodes are amplified by MEA1060 filter amplifiers with custom bandwidth and gain, which are built very small and compact using SMD (Surface Mounted Devices) technology. The small-sized MEA1060 amplifier combines the interface to the MEA probe with the signal filtering and the amplification of the signal. The compact design reduces line pick up and keeps the noise level down. All MEA1060 amplifiers are available either for **inverted** microscopes or for **upright** microscopes, MEA1060-Inv and MEA1060-Up, respectively.

The analog input signals are then acquired and digitized by the MC_Card that is preinstalled on the data acquisition computer.

68-pin MCS high grade cables C68x3M (3 meters), C68x1M (1 meter), or C68x0.5M (0.5 meter) are used for connecting the MEA1060 amplifier, the MC_Card, and any additional devices. The computer supplies the power for the amplifiers via the **isolated power supply IPS10W** (for one amplifier and MEA60-System, or two amplifiers and MEA120-System). The supply power is distributed to the amplifiers via the MCS high grade cable as well. Please note that you need an **external power supply** if you use a MEA switch for operating multiple amplifiers.

Recorded data is graphed, analyzed, and reviewed with the powerful and easy-to-use **MC_Rack** program. You can export the data in standard formats to other programs with the **MC_DataTool**.

2.2 System Configurations and Optional Components

Multi Channel Systems provides several complete standard configurations and custom systems. This chapter will give you an overview on different system configurations. Please see also the handout **Microelectrode Array Systems System Suggestions**, which shows diagrams of several typical setups.

Please note that you have various options for setting up your personal MEA-System configuration. For more information about the scope of delivery of your system, please see the separate please see the separate shipping documents.

Please see the separate documentation for information on installing and operating the individual components of your MEA-System. All warnings and safety related information of the separate documents apply and must be regarded.

Do not hesitate to contact MCS or your local retailer if you are interested in a particular setup or if you have other questions.

2.2.1 Single Components for Standard Systems

The following components are part of MEA standard systems. Please make sure that you have carefully studied the documentation on the single components before setting up your system. All manuals can be found on the installation volume shipped with the system. Updated versions can also be downloaded from the MCS web site.

Web link to the Manuals download page on www.multichannelsystems.com

<i>Product</i>	<i>Manual / Reference</i>
MEA probes of your choice	MEA Manual
Temperature controller TC01 or TC02	TC01/2 Manual
Perfusion cannula PH01 with programmable fluid temperature (systems with enhanced perfusion E only)	PH01 Manual
MEA1060 amplifier(s) with custom bandwidth and gain settings	MEA Amplifier (with Blanking Circuit) for Upright/Inverse Microscopes Manual, MEA_Select Help
MEA Switch (MEA60-2-Systems and MEA120-4-Systems only)	MEA Switch Manual, MEA_Switch Help
Data acquisition computer with MC_Card and integrated isolated power supply IPS10W or external power supply PS40W	MEA-System Manual
Data acquisition and analysis software MC_Rack and MC_DataTool	MC_Rack Manual / Help, MC_Rack Tutorial
Complete MEA-System / Setup	MEA-System Manual, Microelectrode Array Systems — Suggested Setups, MEA Application Notes

2.2.2 Enhanced Perfusion System (-E)

A perfusion system is required especially for recordings from acute slices. All systems can be upgraded with an enhanced perfusion system (indicated by the code –E), featuring a perfusion cannula PH01 with programmable fluid temperature and a two-channel temperature controller TC02 for controlling both the MEA culture chamber temperature and the fluid temperature in parallel.

2.2.3 MEA1060-BC Amplifier with Stimulus Artifact Suppression

All systems are available with MEA1060-BC amplifiers with blanking circuit featuring stimulus artifact suppression. Electrodes can be selected for recording or stimulation with the **MEA_Select** program.

2.2.4 MEA60- and MEA120-System

The **MEA60-System** is a complete system for *in vitro* recording from microelectrode arrays (MEAs), temperature control, and data acquisition from up to 60 electrodes plus 3 additional analog and 3 additional digital input bits. The data acquisition card can convert up to 64 analog channels, or 63 analog channels and 1 digital channel in total.

The **MEA120-System** has a MC_Card extension that allows recording from two MEAs and two MEA1060 amplifiers with 120 electrodes in total plus 3 additional analog and 3 additional digital input bits. The data acquisition card can convert up to 128 analog channels, or 127 analog channels and 1 digital channel in total.

2.2.5 MEA Switch for Using Additional Amplifiers

You can use a **MEA Switch MEAS2/1** to select up to 60 channels from two MEA1060 amplifiers with a MEA60-System. The MEA Switch is very useful for exploiting your MEA-System even more efficiently, as often not all MEA electrodes show signals of interest. Choose any of the up to 60 (120) recording channels conveniently by mouse-click with the MEA_Switch software.

With a **MEA120-System** and a **MEA Switch MEAS4/2**, you can even record from four MEAs simultaneously.

2.3 Accessories

MCS provides a wide range of accessories that will make your MEA-System even more efficient and convenient to use. All accessories are perfect for use with MCS products, but are easily adaptable to custom systems as well. Some accessories are included in complete systems, other have to be ordered separately.

- **1- or 2-channel Temperature controller** for MEAs and for **perfusion cannula PH01**
- **The SD-MEA Signal Divider** allows you to connect any channel via BNC connector to an external device, for example, an oscilloscope, without interrupting the data acquisition.
- **Digital in/out extension** for connecting other devices to single digital input and output channels of the MC_Card via BNC connectors (up to 16 inputs and 16 outputs), for example, for synchronizing stimulation and recording, or for applying feedback.
- **Magnetic plates** and plates with **M3 threads** for positioning and tightly fixing tools next to the MEA.
- **External power supply PS40W** for use with the MEA Switch or for custom setups.

2.4 Add-ons for Stimulation

MCS provides general-purpose stimulators like the advanced **4000 series** with **2, 4** or **8** channels.

The flexible **MC_Stimulus software** enables complex stimulus waveforms (both **current** and **voltage**). Waveforms designed in the program or imported from an external file are converted by the STG into pulses, which are sent to stimulating electrodes.

Stimulus isolation units are integrated in the STG for each channel. Thus, no additional stimulus isolations units are required.

Trigger in- and outputs are available for an exact timing of stimulation and for controlling other instruments by TTL pulses. For example, stimulation and recording can be synchronized with a digital trigger signal (TTL) sent from the Sync Out output of the stimulus generator to the MC_Card via digital inputs.

With the advanced MEA preamplifier with **blanking circuit (BC)**, you will be able to ground electrodes or select electrodes for recording and stimulation by software controls from the data acquisition computer. Stimulus artifacts and amplifier saturation are effectively prevented with a blanking circuit.

2.5 Setting up the MEA-System



Warning: Please read the separate manuals of all individual instruments before installation, especially the warnings and safety information. Make sure all devices are switched off before you connect them to the power supply. Damage to the devices and even fatal injuries may result from improper installation or use.

See also the documentation **Microelectrode Array Systems — System Suggestions** with detailed diagrams and various setup suggestions. Provide a power supply in the immediate vicinity of the installation site.

Note: Do not mismatch the three clearly labeled digital and analog inputs. Digital inputs are for connecting TTL sources (generally used for triggering the recording); analog inputs are for connecting additional analog data sources that are not amplified by the MEA amplifier, for example, for monitoring the temperature, or for recording patch-clamp data in parallel to the MEA recording.

1. Place all devices on a stable and dry surface, where the air can circulate freely and the devices are not exposed to direct sunlight.
2. Set up the computer.
3. Set up all system components as described in the separate manuals.
4. Connect the MEA amplifier to the MC_Card (input labeled MC_Card Ch. 01–64) with 3 m 68-pin MCS standard cable C68x3M. If you use a MEA Switch, please connect the amplifiers to the MEA Switch with 1 m 68-pin MCS standard cables C68x1M, and connect the MEA Switch to the MC_Card with 3 m 68-pin MCS standard cables C68x3M.
5. If you have a MEA120-System, connect the second MEA amplifier with the 68-pin MCS standard cable C68x3M to the input for channels 65–128 labeled MC_CX64 Ch. 65–128. If you use a MEA Switch, please connect the amplifiers to the MEA Switch with 1 m 68-pin MCS standard cables C68x1M, and connect the MEA Switch to the MC_Card with 3 m 68-pin MCS standard cables C68x3M.
6. Optional: Connect other not amplified analog input sources to the BNC connectors labeled Analog IN (1, 2, 3).

7. Optional: Connect digital (TTL) input sources to the BNC connectors labeled Digital IN (Bits 0, 1, 2). If you have only one instrument for triggering recording (for example the Sync Out of a stimulus generator), connect it to bit 0. In MC_Rack, add a Trigger Detector to your virtual rack, and select the Digital Data D1 input stream as the Trigger. Select the appropriate logical state (generally HIGH) for triggering. Mask all unused bits. The standard settings of the Trigger Detector are for using bit 0.
8. Optional: If you have a digital in / out extension, you can connect up to 16 digital input sources and up to 16 devices that you want to be triggered by the Digital Output instrument of MC_Rack.

2.6 Supply Power and Recommended Setups

In the standard MEA-System, the isolated power supply IPS10W that is preinstalled on the data acquisition computer delivers the power for the amplifiers, distributed via the 68-pin MCS high grade cable. One of the limiting factors when using the IPS10W is the voltage drop of the 3 m MCS high grade cable. The characteristic resistance of the cable is 0.3 Ohms per meter. This results in a 1 Ohm resistance for a 3 m cable, leading to a voltage drop of 500 mV for a 500 mA current ($U = R \cdot I = 1 \Omega \cdot 500 \text{ mA} = 500 \text{ mV}$). As the voltage drop limit is 500 mV, the limit for each cable is $\pm 500 \text{ mA}$, that equals 1 MEA amplifier with blanking circuit.



Warning: Follow the manufacturer's setup recommendations. Do not use longer cables than recommended. Do not connect other amplifiers or more amplifiers than recommended. A voltage drop exceeding the limit of $\pm 500 \text{ mA}$ can lead to improper behavior of the amplifier, or can even melt the wire!

The following tables show you how much power the amplifiers need, and how much power the MCS power supplies will provide.

	MEA1060-INV	MEA1060-UP	MEA1060-INV-BC	MEA1060-UP-BC
Supply voltage	$\pm 6 \text{ VDC}$ to $\pm 9 \text{ VDC}$		$\pm 6.5 \text{ VDC}$ to $\pm 9 \text{ VDC}$	
Supply current	max. 220 mA, typically $\pm 150 \text{ mA}$		$\pm 550 \text{ mA}$	

	IPS10W (internal power supply)	PS40W (external power supply)
Output voltage	$\pm 6.3 \text{ V} \pm 10\%$	$\pm 7 \text{ V} \pm 10\%$
Output current	max. 1.2 A @ + 6.3 V or – 6.3 V	max. 2.5 A @ $\pm 7 \text{ V}$

The following table shows the recommended setups regarding the power supplies that are needed for operating these Systems. It is necessary to use an external power supply for operating a MEA Switch (MEAS2to1 or MEAS4to2).

MEA1060-INV/UP	MEA1060-INV/UP-BC	MEAS2/1	MEAS4/2	IPS10W	PS40W	MEA-System
1				1		60
	1			1		60
2				1		120
	2			2		120
2		1			1	60
	2	1			1	60
4			1		1	120
	4		1		1	120

3 Extracellular Recording from MEAs

3.1 Introduction

Over the last 30 years, non-invasive extracellular recording from multiple electrodes has developed into a widely used standard method. Systems and methods have been greatly improved, leading to more features, higher throughput, and lower costs. Almost all excitable or electrogenic cells and tissues can be used for extracellular recording *in vitro*, for example, central or peripheral neurons, heart cells, retina, or muscle cells.

3.2 Background

The semi permeable lipid bilayer cell membrane separates different ion concentrations (charges) on the inner and outer side of the membrane. Therefore, the cell membrane has the electrical properties of a plate capacitor. The electrochemical gradient results in a membrane potential that can be measured directly with an intracellular electrode. When ion channels are opened due to chemical or electrical stimulation, the corresponding ions are moving along their electrochemical gradient. In other words, the resistance of the membrane is lowered, resulting in an inward or outward flow of ions, measured as a transmembrane current.

The extracellular space is conductive as well, and though the resistance is very low, it is not zero. According to Ohm's law ($U=R \cdot I$), the extracellular current results in a small voltage that can be measured with extracellular electrodes. Extracellular signals are smaller than transmembrane potentials, depending on the distance of the signal source to the electrode. Extracellular signal amplitudes decrease with increasing distance of the signal source to the electrode. Therefore, a close interface between electrode and cell membrane is very important for a high signal-to-noise ratio.

The transmembrane current and the extracellular potential follow the same time course and are roughly equal to the first derivative of the transmembrane potential.

A microelectrode array (MEA) is an arrangement of several (typically 60) electrodes allowing targeting several sites for stimulation or recording at once.

The following components are important for an extracellular recording system:

- Signal source (cells / tissue)
- Cell / sensor interface
- Biosensor (MEA)
- Filter amplifier (MEA1060)
- Recording hardware (MC_Card) and software (MC_Rack)

3.3 Signal Types

3.3.1 Single Unit Activities

Usually several cells are plated onto a MEA. The waveform of a single unit spike depends on the signal source, the geometry of the extracellular space, and the distance of the signal source to the electrode. The property of a waveform derived from a single neuron is reproducible over time and therefore specific for that neuron. That is, the differences of waveforms from separate signal sources can be used to distinguish the activities and to sort spikes into single unit spikes. Thus, you can acquire single unit data from multiple cells in parallel by recording from a single electrode.

You have to discriminate between independent activities and network responses. Responses of cells on a MEA triggered by a chemical, electrical, or light stimulus can be either statistically independent or show a specific pattern. The latter is quite interesting for studying the role of cells and different tissues in a pathway. MEA recording allows such studies under controlled experimental settings and is much easier and less labor intensive than an *in vivo* experiment.

3.3.2 Local Field Potentials

If the dendrite soma axes of the active cells are aligned, the waveforms from multiple units on a MEA overlay and form a compound potential, or local field potential (LFP). The higher the activity, that is, the spike rate, the higher is the amplitude of the LFP. A modulation of the stimulus results in a higher frequency of action potentials that will result in a graded multi-unit response. LFPs often show a high signal-to-noise ratio, which is very beneficial for the analysis.

If dendrites are arranged in a nonparallel or radial fashion forming a closed field, the waveforms may cancel each other out, when the neurons fire in synchrony.

3.4 Recording and Stimulation

The MEA sensor is placed directly into the small-sized MEA amplifier. When the amplifier is closed, the contact pins in the lid of the amplifier are pressed onto the MEA contact pads. The very close location of the amplifier to the MEA sensor is very favorable concerning a high signal-to-noise ratio. The amplifier is connected with a single cable to the data acquisition computer.

You can then simply ground bad or unwanted electrodes by toggling small switches on the amplifier. You can also connect a stimulus generator to any electrode(s) for stimulation. Stimulating electrodes are grounded to prevent a saturation of the amplifier.

If you use the new MEA preamplifier with blanking circuit, software controls allow you to select any electrode on a MEA for stimulation and recording. A user defined, typically 500 μ s long, blanking signal switches off stimulating electrodes during stimulation and thus removes stimulus artifacts.

With the MEA_Select software, it is easy to change the electrode selection during the experiment, for example, to use stimulating electrodes for recording and vice versa. It is also possible to use the same electrode for recording shortly after stimulation provided that you use a dedicated biphasic pulse protocol that compensates for the slight DC offset that a stimulating electrode always shows after stimulation.

3.4.1 Microelectrode Arrays (MEAs)

The recording field of a standard MEA is a square grid of 8x8 electrodes with a total length between 120 µm to 5 mm, in the middle of a circular (about 2 cm wide) recording / culture chamber.

The layout of the MEA electrodes follows the scheme of a standard grid: The first digit is the column number, and the second digit is the row number. For example, electrode 23 is positioned in the third row of the second column. The numbering follows the standard order from left to right, and from top to bottom. This numbering is used in the documentation of the MEAs, the MEA1060 amplifiers, and in MC_Rack. That means, if you want to record data from electrode 23, you choose channel 23 for setting up the channel layout map in MC_Rack. Please make sure that the appropriate 2-dimensional data source setup 2 dim. (MEA) for a MEA60-System and MEA120-System has been selected in MC_Rack. For more details, please refer to the MC_Rack Help or Manual.

Microelectrode arrays are available in various configurations:

- Different electrode layouts (8x8, 6x10, High Dense 2x(5x6), 4 Quadrants, Hexa)
- Different electrode diameters and spatial resolutions
- Different electrode materials (Titanium nitride, gold, platinum)
- Opaque (titanium) or transparent (indium tin oxid) tracks

For more information on MEA types, electrode layouts, MEA handling, coating and cleaning, please refer to the MEA Manual.

3.4.2 Signal Amplification and Filters

The standard MEA amplifier combines the probe interface with a band pass filter and the signal amplification in one instrument.

The MEA1060-BC amplifier with blanking circuit is a 60-channel preamplifier with a broad bandwidth. Filter specifications and gain are defined by the following filter amplifier.

Different filter settings are used to enhance the signal-to-noise ratio. The pass band of the filter amplifier depends on the signal type. It is generally useful to filter the data with a cutoff at the highest signal frequency.

For slow signals like field potentials, a bandwidth of 1 to 300 Hz is appropriate. If you like to record fast signals like spikes, a pass band of 300 Hz to 3 kHz is suitable. Cardiac signals have fast and slow components; therefore, you usually need a wider bandwidth of 1 Hz to 3 kHz.

Multi Channel Systems provides custom amplifiers with a bandwidth of your choice, from 0.1 Hz to 10 kHz. Please note that it is often wise to acquire the data with a broadband amplifier and use the digital filter of the free MC_Rack program to change the pass band and filter the raw data. This way, you are much more flexible in designing your experiments. As a further advantage, you can see the original (not filtered) data as well. This is especially important because all filters are known to distort signals. On the other hand, you may need a higher sampling rate to avoid aliasing, and the signal-to-noise ratio is lower. See also the chapter "Data Acquisition" for more information.

The standard gain of a MEA amplifier is 1200, which is fine for most applications, but MCS can also provide amplifiers with a gain of your choice (from 100 to 5000) as well. For large signals (for example, from heart preparations), you need a lower gain to prevent a saturation of the amplifier. Please note that the gain is a fixed hardware property; and that you cannot change the gain of the amplifier by software controls.

Please note that the ratio of the output signal to the input signal, that is, the gain, is not a fixed parameter for the complete bandwidth. The gain that was specified for the amplifier, for example, 1200, is not fully reached at the borders of the amplifier's pass band. The general rule is, that at the lower and upper limit of the frequency band, the gain is $\sqrt{2}/2$, that is approximately 70 %, of the full gain. Therefore, you should use a bandwidth that is at a safe distance of the signals of interest. Outside the pass band, the gain decreases with the frequency and finally approaches zero.

The low-pass filter properties of the MC_Card will affect the bandwidth of the complete system only slightly.

For information on the gain and filters of the MEA amplifiers, please see the appropriate MEA Amplifier Manual. For more information on gain and filters in general, please refer to standard literature or contact your local retailer.

3.4.3 Data Acquisition

Recording from up to 128 channels is easy with the **MC_Card hardware** and the **MC_Rack software**.

MC_Card hardware

Important: You need to have installed the latest MC_Card driver to operate the MC_Card, which is usually preinstalled on the data acquisition computer. The installation may be invalid if the MC_Card does not respond. Please contact Multi Channel Systems if you need the MC_Card Driver and a description of the installation.

The MC_Card is an A / D board that converts analog signals in real time into digital data streams at sampling rates of up to 50 kHz for all channels.

You configure the input voltage range from +/- 400 mV to +/- 4V and the sampling rate with the software controls in the MC_Rack program. Please refer to the MC_Rack Help or Manual for more information.

The input voltage range affects your dynamic range, that is, the lower the input voltage range, the higher is the voltage resolution.

Please see the MC_Card data sheet for additional information on the pin layouts and the technical specifications.

DC Offset correction

An offset correction is generally not necessary, because the intrinsic DC offsets of the MCS amplifier outputs and the MC_Card are very low in comparison to the signals of interest. The maximum total DC offset is +/- 3 mV (+/- 2 mV for the MC_Card, +/- 1 mV for the MEA amplifier outputs). For a standard MEA amplifier with a standard gain of 1200, this results in a maximum offset of only 2.5 μ V (+/- 3 mV divided by 1200) with respect to the input signals.

You can use the MC_Rack offset correction feature to remove even this low offset and reset all channels to zero. Please refer to the MC_Rack Help or Manual for more information.

Note: If you observe a large offset on any channel(s), you should contact your local retailer for troubleshooting. The offset correction is not intended for removing large offsets, because the offset correction will decrease the input voltage range.

Sampling rate

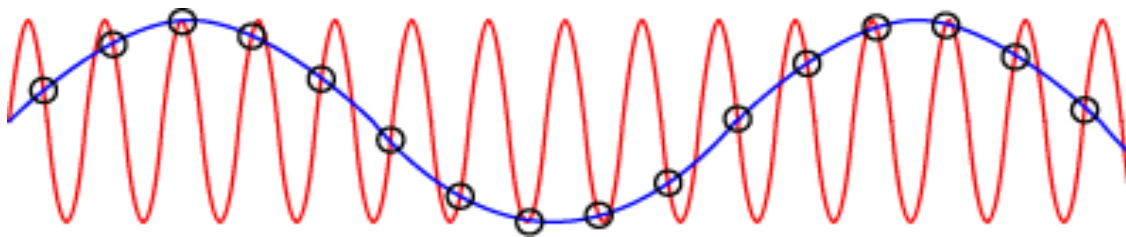
It is recommended to adjust the sampling rate according to your signals, because the higher the sampling rate, the bigger the file size will be.

As a rule of thumb, the sampling rate should equal five times the highest signal frequency for a good digitized representation of the continuous analog signals. If the sampling rate is too low, you will miss signals and / or see artifacts. Considering the preceding statements about filtering data, you would for example use a 5 kHz sampling rate when using a MEA amplifier with a cutoff frequency of 1 kHz.

Please note that if you use a broadband amplifier and a digital filter, you may have to use an even higher sampling rate.

This is the case because the whole amplifier bandwidth is recorded and then high frequency noise is removed with a digital Low Pass filter after recording. Frequencies (noise) that are above half the sampling rate (for example above 2.5 kHz at a 5 kHz sampling rate) will be transformed into lower frequencies. This is called aliasing. This low frequency noise passes the digital Low Pass filter and increases your noise level.

According to the Nyquist-Shannon sampling theorem, the sampling rate should equal twice the bandwidth of the analog (hardware) Low Pass filter. The 1/2 bandwidth frequency is also called Nyquist frequency. You may ignore this if saving hard disk space is more important for your application than the noise level.



Aliasing

Note: The sampling frequency should be at least **five times** the highest signal frequency **and** at least **twice** the bandwidth of the MEA1060 amplifier.

Example:

You have a broadband MEA1060 amplifier with a bandwidth of 0.1 Hz to 10 kHz. The expected signals have a maximum frequency of 1 kHz. Therefore, you want to filter the data with a digital Low Pass filter and a cutoff frequency of 1 kHz. A sampling rate of 5 kHz (five times the highest signal frequency) would be required for faithfully reproducing the signals, but you should use a sampling rate of at least 20 kHz because the sampling rate should equal twice the bandwidth of the analog filter, regardless of the digital filter properties.

If you have a MEA1060 amplifier with a cutoff frequency of 1 kHz instead, no digital filter would be required, and a sampling rate of 5 kHz would be enough.

Software package

With the high-performance data acquisition and analysis program **MC_Rack**, you can flexibly manage all data streams. For example, you can display the raw data of all channels while recording only the raw data of the channels of interest and the extracted parameters of all channels. This saves computer performance and hard disk space.

MC_Rack is not limited to special applications, but can be flexibly adapted to a wide range of applications.

Unlimited software licenses and support come free with the MEA-System, and free software updates lower the costs as well.

The *.mcd data format is supported by several third party programs for further analysis. You can also easily convert recorded data to universal formats such as ASCII with the **MC_DataTool** program.

3.5 Using the Additional Analog Inputs

The additional analog inputs A1, A2, A3 are intended for recording additional information from external devices, for example, for recording patch clamp in parallel to the MEA recording, for monitoring the temperature, or for recording voice. You could also use the analog inputs for triggering the MC_Card, but please note that the digital inputs are intended for accepting TTL pulses.

As the gain is generally completely different on the electrode inputs and on the additional analog inputs, signals on the analog channels are recorded "as is", with no respect to the gain specified in MC_Rack.

Recording Voice on Analog Inputs

Microphones do not generate enough voltage to directly connect them to the analog inputs. You need to use some kind of amplifier that adapts the output voltage of the microphone to the input voltage range of the MC_Card.

You can then use the MC_Rack **Sound** tool for replaying the recorded voice. Please see the MC_Rack Manual for more information.

3.6 Digital Input / Output, System Synchronization

TTL stands for Transistor-Transistor Logic. A TTL pulse is defined as a digital signal for communication between two devices. A voltage between 0 V and 0.8 V is considered as a logical state of 0 (LOW), and a voltage between 2 V and 5 V means 1 (HIGH).



Warning: A voltage that is higher than +5 Volts or lower than 0 Volts, that is, a negative voltage, applied to the digital input would destroy the MC_Card. Make sure that you apply only TTL pulses (0–5 V) to the digital inputs.

Important: In the standard configurations of the MEA-System, only 3 BNC connectors are included for the digital input bits 0 to 2. If you want to use more bits of the 16-bit input channel or the 16-bit output channel (as described in chapter Triggering other Instruments by the MC_Card), you have to order a digital in / out extension separately. You can also upgrade your MEA-System with the extension later. Please contact your local retailer for details.

3.6.1 Triggering the MC_Card and MC_Rack

The digital input accepts TTL pulses. This feature can be used for triggering the MC_Card and MC_Rack, for example, for synchronizing stimulation and data acquisition.

For example, you can connect the Sync Out of a STG (stimulus generator) to one of the digital input bits. If you use only one instrument for triggering, connect it to bit 0. In MC_Rack, add a **Trigger Detector** to your virtual rack, and select the **Digital Data D1** input stream as the **Trigger**. Select the appropriate logical state (generally HIGH) for triggering. Mask all unused bits. The standard settings of the Trigger Detector are for using bit 0.

Please see the documentation on the **Recorder** and on the **Trigger Detector** instrument and on triggered data in the MC_Rack Help or Manual for more details.

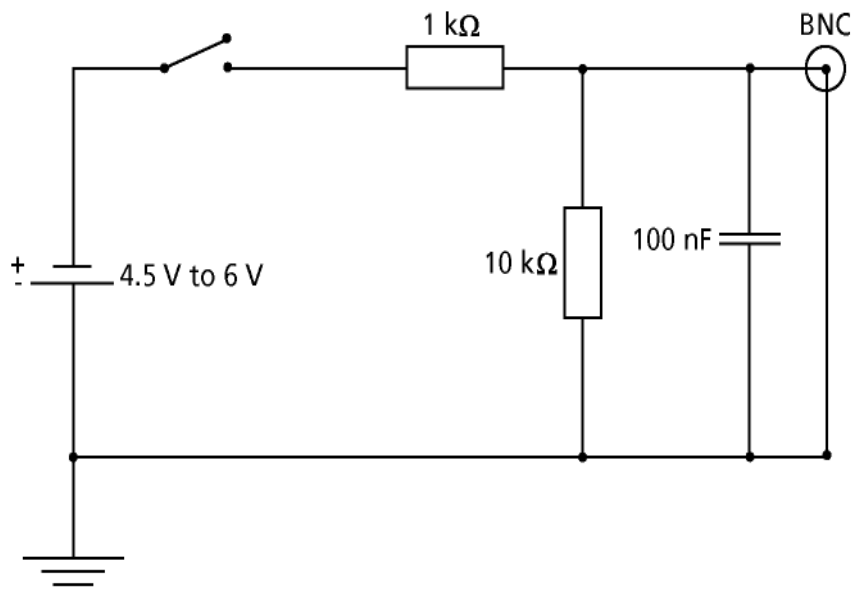
Important: It is recommended to apply TTL pulses with a duration of at least 200 μ s. Shorter pulses may be ignored by the MC_Card. Please mask unused (not connected) digital input channels in the MC_Rack program to ignore undefined states of the open inputs that can cause unwanted trigger events. Please see the MC_Rack Manual for more details.

3.6.2 Custom Switch for "Remote-Controlling" of the MC_Card

You can connect any device that produces TTL outputs, for example a switch, to one of the digital input bits of the MC_Card. This means you can use a trigger for remote controlling the recording with MC_Rack, or for synchronizing systems, if the data acquisition computer is not within reach during an experiment.

You can define the time length of the cutouts that are recorded around the trigger event in MC_Rack. Please note that it is not possible to start the recording of a continuous data file with MC_Rack on a trigger, but you can start a new data file on the trigger event (select the Recorder option Create New File On Trigger).

The following picture shows a suggested circuit diagram for a switch used for remote controlling. The resistor and capacitor work as a low-pass filter on the TTL signal and are necessary to reduce ringing of the signal.



3.6.3 Triggering other Instruments by the MC_Card

The digital output of the MC_Card sends 20 ms TTL pulses (0 V = LOW and 5 V = HIGH). This feature can be used to apply a feedback triggered by a signal or a parameter stream.

For example, you can connect the Trigger In of a stimulus generator (STG) to the digital output via the digital in / out extension. You can also use the digital output for a synchronization of the MEA-System with other systems, for example, for Calcium imaging or video tracking (provided that the other system of choice is able to receive TTL pulses).

Please see the documentation on the Digital Output instrument in the MC_Rack Help or Manual for more details.

4 Troubleshooting

4.1 About Troubleshooting

The following hints are provided to solve special problems that have been reported by users. Most problems occur seldom and only under specific circumstances. Please check the mentioned possible causes carefully when you have any trouble with the product. In most cases, it is only a minor problem that can be easily avoided or solved.

If the problem persists, please contact your local retailer. The highly qualified staff will be glad to help you. Please inform your local retailer as well, if other problems that are not mentioned in this documentation occur, even if you have solved the problem on your own. This helps other users, and it helps MCS to optimize the instrument and the documentation.

Please pay attention to the safety and service information in the separate manuals of the related products and in the software help. Multi Channel Systems has put all effort into making the product fully stable and reliable, but like all high-performance products, it has to be handled with care.

4.2 Triggering / Digital Input does not Work

You have connected a TTL source (for example, the Sync Out of a stimulus generator) to the digital input of the MC_Card, and configured the virtual rack in MC_Rack for triggering displays or data acquisition by the TTL source, but you do not see any sweeps.

Possible causes:

- ? You have mismatched the digital input with the analog input. To test this, please add a **Digital Display** to your virtual rack. You should see the trigger event as a logical state of HIGH (=1). If you cannot see any signals, please add a Data Display to your rack and select the analog raw data as the input stream. Make sure the channel layout map of the display shows all 3 analog input channels (A1–A3). If you have mismatched the inputs, you will now see the (clipped) trigger events.
- Connect the TTL source the BNC connectors labeled **Digital IN (Bits 0, 1, 2)**. If you have only one instrument for triggering recording (for example the Sync Out of a stimulus generator), connect it to bit 0.
- If you use a **digital in / out extension (Di/o)** accessory, you can connect up to 16 digital input sources and up to 16 devices that you want to be triggered by the **Digital Output** instrument of MC_Rack.
- ? The TTL source does not generate true TTL signals (5 V), or the TTL pulse is shorter than 200 µs.
- The MC_Card can only accept TTL signals (CMOS 5 V TTL level) as a digital input stream. A minimum TTL pulse of 200 µs is recommended. Otherwise, a detection of the trigger by the MC_Card is not guaranteed.
- ? The software settings for the **Trigger Detector** do not match with the hardware configuration.
- In MC_Rack, add a Trigger Detector to your virtual rack, and select the Digital Data D1 input stream as the Trigger. Check the digital inputs and make sure that the same bit input that is connected is selected in the software. (The standard settings of the Trigger Detector are for using bit 0.) Mask all unused bits. Select the appropriate logical state (generally HIGH) for triggering. Please see the MC_Rack Help or Manual for more details.

4.3 Artifacts caused by Perfusion

You observe artifacts or an increased noise level after you started the perfusion.

Possible causes:

- ? The artifacts correlate with an oscillation of the liquid level. The oscillation will cause the artifacts, and also mechanically stress the biological sample.
- Use a bevelled tip for the perfusion in- and outlet. If the tip of the perfusion outlet has a blunt end, there will be no continuous liquid flow, but instead, the following can be observed: The liquid level will rise until it reaches the blunt tip; a discrete volume of liquid will be aspirated in a short moment; the liquid level will rise again, and so on, leading to an oscillation. The tip should be cut in an angle of about 45°. You can also use commercially available metal needles with a bevelled tip.
- ? The perfusion is not appropriately grounded.
- Connect the perfusion line to the ground of the amplifier / setup. You should consider using a metal cannula that can directly be connected to ground for the perfusion inlet and outlet. You could also insert a metal wire that is connected to ground into the tubing.
- ? The aspiration pump is oscillating.
- MCS recommends the use of a peristaltic pump for an open perfusion system. The more rollers the pump head has, the lower are the oscillations of the fluid flow. For a continuous perfusion in a closed system, you can also use an infusion-withdrawal syringe pump.

5 Appendix

5.1 Contact Information

Local retailer

Please see the list of official MCS distributors on the MCS web site.

User forum

The **Multi Channel Systems User Forum** provides an excellent opportunity for you to exchange your experience or thoughts with other users worldwide.

Web link to the User Forum

Mailing List

If you have subscribed to the mailing list, you will be automatically informed about new software releases, upcoming events, and other news on the product line. You can subscribe to the list on the contact form of the MCS web site.

www.multichannelsystems.com

5.2 Ordering Information

Please contact your local retailer for pricing and ordering information.

5.2.1 MEA-Systems

Product	Product Number	Description
MEA recording-System for inverted microscopes, 60 electrode channels	MEA60-Inv-System	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Inv amplifier, TC01, power supply, and accessories
MEA recording-System for inverted microscopes, 60 electrode channels, 2 MEA amplifiers	MEA60-Inv-2-System	Complete with 5 MEAs, data acquisition computer with MC_Card, 2 x MEA1060-Inv amplifier, MEAS2/1, TC02, power supply, and accessories
MEA recording-System for upright microscopes, 60 electrode channels	MEA60-Up-System	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Up amplifier, TC01, power supply, and accessories
MEA recording-System for upright microscopes, 60 electrode channels	MEA60-Up-2-System	Complete with 5 MEAs, data acquisition computer with MC_Card, 2 x MEA1060-Up amplifier, MEAS2/1, TC02, power supply, and accessories
MEA recording-System for inverted microscopes with advanced perfusion, 60 electrode channels	MEA60-Inv-System-E	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Inv amplifier, TC02, PH01, power supply, and accessories
MEA recording-System for inverted microscopes with advanced perfusion, 60 electrode channels	MEA60-Inv-2-System-E	Complete with 5 MEAs, data acquisition computer with MC_Card, 2 x MEA1060-Inv amplifier, MEAS2/1, 2 x TC02, 2 x PH01, power supply, and accessories
MEA recording-System for upright microscopes with advanced perfusion, 60 electrode channels	MEA60-Up-System-E	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Up amplifier, TC02, PH01, power supply, and accessories
MEA recording-System for upright microscopes with advanced perfusion, 60 electrode channels	MEA60-Up-2-System-E	Complete with 5 MEAs, data acquisition computer with MC_Card, 2 x MEA1060-Up amplifier, 2 x TC02, 2 x PH01, power supply, and accessories
MEA recording-System for inverted microscopes, 120 electrode channels	MEA120-Inv-System	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Inv amplifier, TC02, power supply, and accessories
MEA recording-System for inverted microscopes, 120 electrode channels	MEA120-Inv-4-System	Complete with 5 MEAs, data acquisition computer with MC_Card, 4 x MEA1060-Inv amplifier, MEAS4/2, 2 x TC02, power supply, and accessories
MEA recording-System for upright microscopes, 120 electrode channels	MEA120-Up-System	Complete with 5 MEAs, data acquisition computer with MC_Card, MEA1060-Up amplifier, TC02, power supply, and accessories
MEA recording-System for upright microscopes, 120 electrode channels	MEA120-Up-4-System	Complete with 5 MEAs, data acquisition computer with MC_Card, 4 x MEA1060-Up amplifier, MEAS4/2, 2 x TC02, power supply, and accessories

5.2.2 MEA Amplifiers

Product	Product Number	Description
MEA amplifier for inverted microscopes	MEA1060-Inv	Probe interface and 60 channel pre- and filter amplifier with custom gain and bandwidth
MEA amplifier for upright microscopes	MEA1060-Up	
MEA amplifier with blanking circuit for inverted microscopes	MEA1060-Inv-BC	Probe interface and 60 channel pre- and filter amplifier with custom gain and bandwidth. The blanking circuit prevents the amplifier from getting saturated and thus prevents stimulus artifacts.
MEA amplifier with blanking circuit for upright microscopes	MEA1060-Up-BC	

5.2.3 Accessories

Product	Product Number	Description
Holder with M3 threads	MPM3	For fixing tools with M3 threads next to the MEA
1-Channel temperature controller	TC01	PID based technology, set-point temperature reached fast within 30 s to 5 minutes, control temperature range from ambient temperature to +50 °C
2-Channel temperature controller	TC02	
Perfusion cannula with programmable fluid temperature	PH01	Temperature can be programmed with the temperature controller TC01 or TC02
Signal divider for MEA-Systems	SD-MEA	Placed between a MEA1060 amplifier and MC_Card, permits to select any channel, does not interfere with the data acquisition, for example for connecting an oscilloscope or other devices to single channels
MEA Switch for 4 amplifiers	MEAS4/2	The MEA Switch allows you to acquire data from 60 single channels from two MEA1060 amplifiers. If you have a 128-channel MC_Card (MEA 120-System), you can even pick 128 channels in total from two MEA pairs with the MEA Switch for four amplifiers MEAS4/2. The selected channels are combined to one Electrode Raw Data stream that is delivered to MC_Card by a 68 pin MCS High Grade Cable.
MEA Switch for 2 amplifiers	MEAS2/1	
Digital in/out extension	Di/o	For connecting other devices to single digital input and output channels of the MC_Card via BNC connectors (up to 16 inputs and 16 outputs), for example for synchronizing stimulation and recording, or for applying feedback.
Isolated power supply with 10 W power and ± 6.3 V output voltage	IPS10W	Isolated power supply for integration into the data acquisition computer. For supplying power to MEA1060 amplifiers.

5.2.4 Stimulus Generators

Product	Product Number	Description
2-Channel stimulus generator	STG4002	4000 series: General-purpose stimulus generator for current and voltage-driven electrical stimulation, with integrated stimulus isolation unit for each output channel. Operating in Download and Streaming mode (continuous downstreaming of pulses from connected computer). MC_Stimulus II program with advanced features.
4-Channel stimulus generator	STG4004	
8-Channel stimulus generator	STG4008	